CLAIMS

1. A water insoluble nanoparticle comprising at least one neutron capture element in an inorganic form for use in therapy, surgery or diagnosis.

2. A water insoluble nanoparticle comprising at least one neutron capture element in an inorganic form, said nanoparticle comprising a biocompatible outer layer.

3. A water insoluble nanoparticle as claimed in claim 2 wherein said outer layer is hydrophilic.

4. A nanoparticle as claimed in any preceding claim having a particle size of about 10^{-10} m to about 10^{-6} m.

5. A nanoparticle as claimed in any preceding claim having a particle size of about 10^{-10} m to about 10^{-7} m.

6. A nanoparticle as claimed in any preceding claim having a particle size of about 10^{-9} m to about 10^{-8} m.

7. A nanoparticle as claimed in any preceding claim wherein said at least one neutron capture element is boron, preferably ^{10}B.

8. A nanoparticle as claimed in any of claims 1 to 6 wherein said at least one neutron capture element is selected from the group consisting of ^{6}Li, ^{22}Na, ^{22}Co, ^{113}Co, ^{126}I, ^{135}Xe, ^{148m}Pm, ^{149}Sm, ^{151}Eu, ^{155}Gd, ^{157}Gd, ^{164}Dy, ^{184}Os, ^{199}Hg, ^{230}Pa, ^{235}U, ^{241}Pu.

9. A nanoparticle as claimed in any preceding claim wherein said neutron capture element is in its natural crystalline form.

10. A nanoparticle as claimed in any of claims 1 to 8 wherein said neutron capture element is in a particulate form.

11. A nanoparticle as claimed in any of claims 1 to 8 wherein said neutron capture element is in the form of a glass or a glass ceramic.

12. A nanoparticle as claimed in any of claims 1 to 8 wherein said neutron capture element is in the form of a polymerised inorganic matrix.

13. A nanoparticle as claimed in any of claims 1 to 8 wherein said neutron capture element is in the form of a sol-gel derived xerogel.

14. A nanoparticle as claimed in any of claims 1 to 8 wherein said neutron capture element is in the form of an organically modified ceramic and wherein the element comprises at least one bond to a hydrocarbon chain.

15. A nanoparticle as claimed in claim 7 wherein said boron is in the form of:

(i) $^{10}B_xM_n$;

(ii) $^{10}B_xH_n$; or

(iii) $R\text{-}^{10}B_n\text{-}O_n$

wherein M is a metal or is selected from nitrogen, carbon, oxygen, chlorine, bromine or fluorine, x and n are integers of one or above and R is a hydrocarbon chain or other organic chain.

16. A nanoparticle as claimed in claim 7 or 8 wherein said neutron capture element is in the form of $(X\text{-}O\text{-}X)_n$ wherein n is an integer of 1 or above and X is the neutron capture element.

17. A nanoparticle as claimed in any of claims 1 or claims 4 to 16 further comprising a biocompatible outer layer.

18. A nanoparticle as claimed in any of claims 2, 3 or 17 wherein said biocompatible outer layer does not include intramolecular cross-linkages.

19. A nanoparticle as claimed in claim 17 or claim 18 wherein said biocompatible outer layer is selected from the group consisting of polymers, organic or inorganic pharmaceutical excipients, low molecular weight oligomers, natural products for example, gelatins, gums, fatty acids, soya bean oils or purified fractions thereof, ionic surfactants and non-ionic surfactants.

20. A nanoparticle as claimed in claim 18 wherein said biocompatible outer layer comprises an excipient selected from the group including gelatin, casein, lectine (phosphatides), gum acacia, calcium stearate, cholesterol, tragacanth, sorbitan esters, stearic acid, benzalkonium chloride, glycerol monostearate, cetostearl alcohol, cetomacrogol emulsifying wax, polyoxyethylene alkyl ether, polyoxyethylene castor oil derivatives, polyoxyethylene sorbitan fatty acid esters polyethylene glycols, polyoxyethylene stearates, colloidal silicon dioxide, colloidal titanium dioxide, phosphates, sodium dodecylsulphae, caroxymethycellulose calcium or sodium, methylcellulose, hydroxyrthylcellulose, hydroxypropylmethycellulose phthalate, noncrystalline cellulose, hydroxypropycellulose, magnesium aluminium silicate, triethanoloamine, polyvinyl alcohol (PVA), and polyvinypyrrolidone (PVP).

21. A nanoparticle as claimed in any of claims 17 to 20 wherein said biocompatible outer layer comprises a polymer selected from:-

(i) block copolymers, for example poly(ethylene glycol-aspartate), block copolymers of ethylene oxide and propylene oxide, tetrafunctional block copolymers derived from the addition of ethylene oxide and propylene oxide to ethylene diamine;

(ii) polyethylene glycol (PEG) or ethylene glycol copolymers;

(iii) polysaccharides, e.g. dextrin, dextran, chitosan (N-succinyl chitosan), carboxymethyl chitin, carboxymethyl pullulan or alginate;

(iv) poly (amino acids), for example, poly [N-(2-hydroxyethyl)-L-glutamine) PHEG, β-poly(2-hydroxyethyl aspartamide) PHEA, poly(glutamic acid), polyaspartic acid), polylysine (poly(L-lysine);

(v) polyesters, for example poly (α or β-malic acid);

(vi) alternating polymers, for example, PEG-lysine;

(vii) copolymers of styrene and maleic anhydride;

(viii) polygalacturonic acid;

(ix) copolymers of hydroxalkyl(meth)acrylate e.g. N-phenylpyrrolidone, poly (L-glutamic acid and hydroxyethyl-L-glutamine), poly (α-malic acid), polyaspartic acid-PEG copolymers, poly-L- lysine and copolymers of polyethyleneimine;

(x) poly(α-L-glutamic acid) (PGA);

(xi) biodegradable diamido-diamine polymer; and

(xii) N-(2-hydroxypropyl) methacrylamide (HPMA copolymer)

22. A nanoparticle as claimed in any of claims 17 to 19 wherein said biocompatible outer layer comprises a surfactant selected from aerosol OT (dioctyl ester of sodium sulfosuccinic acid), polyoxyethylene sorbitan fatty acid ester, sodium lauryl sulfate, polyoxyethylene 20 sorbitan monolaurate, polyoxyethylene 20 sorbitan monopalmitate, polyoxyethylene 20 sorbitan monostearate, polyoxyethylene 20 sorbitan monooleate and lecithin N-(2-hydroxypropyl).

23. A nanoparticle as claimed in any preceding claim wherein the neutron capture element is present as a layer or film around an inorganic nanoparticle core.

24. A nanoparticle as claimed in claim 23 wherein said core is selected from mica, zeolites, TiO_2 spheres, ZrO_2 spheres or particles or organic polymer particles or spheres.

25. A nanoparticle as claimed in any preceding claim wherein said particles further comprise a pharmacologically active substance.

26. A nanoparticle as claimed in claim 25 wherein said pharmacologically active substance is loaded into said nanoparticles by absorption, adsorption or incorporation.

27. A nanoparticle as claimed in claim 25 or claim 26 wherein said pharmacologically active substance is a chemotherapeutic agent.

28. A nanoparticle as claimed in any preceding claim further comprising a further metal selected from the group consisting of vanadium (V), manganese (Mn), iron (Fe), ruthenium (Ru), technetium (Tc), chromium (Cr), platinum (Pt), cobalt, (Co), nickel (Ni), copper (Cu), zinc (Zn), germanium, (Ge), indium (In), tin (Sn), yttrium (Y), gold (Au), barium (Ba), tungsten (W), and gadolinium (Gd).

29. A nanoparticle as claimed in claim 28 wherein said further metal is present at a concentration of about 0.0001% wt/wt to about 0.1% wt/wt.

30. A pharmaceutical composition comprising a water insoluble nanoparticle comprising at least one neutron capture element in an inorganic form.

31. A pharmaceutical composition as claimed in claim 30 comprising a water insoluble nanoparticle according to any of claims 2 to 29.

32. The use of water insoluble nanoparticles comprising at least one neutron capture element in an inorganic form in the manufacture of a medicament for use in neutron capture therapy.

33. A use as claimed in claim 32 wherein said neutron capture therapy is for the treatment or ablation of cancer or other diseased tissues e.g. lymphomas, skin cancer, breast cancer, lung cancer, head and neck cancer, bone cancer, prostate cancer, cancer of the pancreas, cervical cancer, brain cancers e.g. glioblastomas, primary and secondary metastases and benign and metastatic prostate cancers, e.g. benign prostate hyperplasia.

34. A use as claimed in claim 33 wherein said tumour is solid and discrete.

35. A use as claimed in any of claims 32 to 34 wherein said neutron capture therapy is administered over a period of one to fourteen days.

36. A use as claimed in any of claims 32 to 35 wherein said nanoparticle is a nanoparticle according to any of claims 2 to 29.

37. A method for neutron capture therapy comprising:

(i) administering a water insoluble nanoparticle having at least one neutron capture element in an inorganic form to an individual;

(ii) allowing said nanoparticles to accumulate at a desired location in the body; and

(iii) administering neutrons to said individual.

38. A method of claim 37 for the treatment or ablation of cancer or other diseased tissues e.g. lymphomas, skin cancer, breast cancer, lung cancer, head and neck cancer, bone cancer, prostate cancer, cancer of the pancreas, cervical cancer, brain cancers e.g. glioblastomas, primary and secondary metastases and benign and metastatic prostate cancers, e.g. benign prostate hyperplasia.

39. A method as claimed in claim 38 wherein said tumour is solid and discrete.

40. A method as claimed in claim 38 or claim 39 further comprising the step of removing a tumour by surgery.

41. A method as claimed in any of claims 38 to 40 further comprising analysing the concentration of the neutron capture element in the target tissue.

42. A method as claimed in claim 41 wherein said analysis comprises MRI, PET or SPECT imaging.

43. The use of water insoluble nanoparticles comprising at least one neutron capture element in an inorganic form in a method for neutron capture therapy.

44. A use as claimed in claim 43 for the treatment or ablation of cancer or other diseased tissues e.g. lymphomas, skin cancer, breast cancer, lung cancer, head and neck cancer, bone cancer, prostate cancer, cancer of the pancreas, cervical cancer, brain cancers e.g. glioblastomas, primary and secondary metastases and benign and metastatic prostate cancers, e.g. benign prostate hyperplasia.

45. A use as claimed in claim 44 wherein said tumour is solid and discrete.

46. A process for the preparation of water insoluble nanoparticles comprising at least one neutron capture element in an inorganic form, said process comprising:

(i) providing at least a first mass of said neutron capture element in an inorganic form;

(ii) providing at least a second mass of the same type of material;

(iii) mixing said first and second masses in the absence of other abrasive material;

(iv) causing frictional abrasion between said first and second masses; and

(v) collecting said nanoparticles.

47. A process as claimed in claim 46 wherein at least one further, non abrasive material is included in said mixing step (iii).

48. A process as claimed in claim 47 wherein said further, non abrasive material is selected from the group consisting of vanadium (V), manganese (Mn), iron (Fe), ruthenium (Ru), technetium (Tc), chromium (Cr), platinum (Pt), cobalt, (Co), nickel (Ni), copper (Cu), zinc (Zn), germanium, (Ge), indium (In), tin (Sn), yttrium (Y), gold (Au), barium (Ba), tungsten (W), and gadolinium (Gd).

49. A process as claimed in any of claims 46 to 48 wherein the resulting nanoparticles are characterised by any of the features of claims 2 to 10 or claims 12 to 27.

50. A water insoluble nanoparticle substantially as hereinbefore described.

51. A pharmaceutical composition substantially as hereinbefore described.

52. A method for neutron capture therapy substantially as hereinbefore described.

53. A process for the preparation of water insoluble nanoparticles substantially as hereinbefore described.